INFLUENZA NANOVACCINE

RELATED APPLICATION

This application claims priority under 35 U.S.C. § 119(e) to U.S. Provisional Patent Application Nos. 62/679,330 filed Jun. 1, 2018 and 62/681,447 filed Jun. 6, 2018, which applications are incorporated herein by reference.

GOVERNMENT SUPPORT

This invention was made with government support under Grant No. R01 AI127565 awarded by the National Institutes of Health. The government has certain rights in the invention.

FIELD OF INVENTION

The present invention relates generally to immunogenic compositions, and more particularly, to an immunogenic composition that may confer protective immunity to a subject against an influenza virus.

BACKGROUND OF THE INVENTION

The influenza virus is an RNA enveloped virus with a particle size of about 125 nm in diameter. The virus generally comprises an internal nucleocapsid or core of ribonucleic acid (RNA) associated with nucleoprotein, surrounded by a viral envelope with a lipid bilayer structure and external glycoproteins. The inner layer of the viral envelope is predominantly composed of matrix proteins and the outer layer mostly composed of host-derived lipid material. The surface glycoproteins neuraminidase (NA) and hemagglutinin (HA) appear as outward radiating appendages or spikes, 10 to 12 nm long, from the surface of the virus particles. These surface proteins, and in particular the hemagglutinin protein, may be used to determine the antigenic specificity of the influenza subtypes.

The influenza family of viruses may be categorized into four serotypes types: A, B, C and D. Influenza A and B viruses cause seasonal epidemics of disease almost every winter in the United States. Influenza type C infections generally cause a mild respiratory illness and are not thought to cause epidemics. The Influenza D viruses primarily affect cattle and are not known to infect or cause illness in people.

Influenza A virus (IAV) may be further categorized according to subtypes based on the variant of hemagglutinin and the neuraminidase expressed on the viral surface. There are 18 different hemagglutinin subtypes (H1-H18) and 11 different neuraminidase subtypes (N1-N11), and each subtype may be further classified into various strains according to the HA an N subtype (e.g., H1N1, H3N1, etc.).

IAV is a common respiratory pathogen that undergoes seasonal antigenic drift continually giving rise to variant strains that may escape existing immune protection. This viral drift detrimentally impacts public health as well as the economy within the United States. For example, during the 2015-2016 flu season, IAV caused approximately 310,000 hospitalizations, 12,000 deaths, and incurred $87 million-dollars in financial burden. Each of these burdens may be exacerbated during years when an antigenic shift event gives rise to pandemic strains further underscoring the need to thwart the spread of IAV.

The most effective way to deal with the influenza virus for the population most at risk of severe complications is through infection prevention. For example, use of an available influenza vaccine is an effective way to lower the mortality rate in a population. However due to the ever-changing nature of the influenza virus, the development of an effective vaccine to protect against the currently circulating virus strains is complex and expensive. Moreover, patient compliance in receiving the vaccine is generally very low. Thus, large numbers of patients at risk of serious complications from influenza virus go unprotected.

Traditional vaccination strategies that have been used to prevent the spread of IAV primarily includes two vaccines: inactivated influenza vaccine (IIV) and live-attenuated influenza vaccine (LAIV). In the 2015-2016 IAV season, IIV and LAIV were estimated to avert 5 million IAV-induced illnesses and 3,000 deaths within the United States alone.

Both IIV and LAIV largely prevent IAV infection by inducing the production of neutralizing antibodies; however, each of the vaccines induce distinctive immune responses due, at least in part, to their disparate formulations and inoculation routes. IIV contains inactivated IAV proteins/virus in the presence or absence of a variety of adjuvants and is administered intramuscularly (i.m.). In contrast, LAIV utilizes a temperature-sensitive attenuated strain of IAV that is given intranasally (i.n.) as a needle-free spray. Despite these differences, both IIV and LAIV provide systemic immunity by inducing IAV-specific antibody (humoral) responses. However, it is less clear if these vaccination strategies generate robust IAV-specific CD4 or CD8 T cell responses, the latter requiring presentation of viral antigens via either direct infection of antigen presenting cells (APC) or cross-presentation. Furthermore, due to its i.m. delivery, IIV is not thought to drive airway-resident effector T cell responses as the nasal mucosa and the lungs are not directly involved in any vaccine induced priming of naive T cells. In contrast, while LAIV is capable of replicating and may induce effector T cell immunity in the upper airway, LAIV is unable to produce local immunity in the lower airway. Thus, even when de novo T cell responses are generated by IIV or LAIV, the tissue localization of these responses suggests that neither would drive long-term T cell memory within the lung airways.

Additionally, recommendations in recent years against the use of LAIV by the Centers for Disease Control and Prevention due to its reduced effectiveness indicates that in some years there is no currently approved vaccine that is needle-free or that induces even limited local immunity within the airways. These vaccine limitations—in combination with IAV disease burden—have resulted in increased efforts in developing innovative IAV vaccination strategies that generate systemic and local immunity within the upper and lower airways of the lungs.

Accordingly, a need exists for an easily administered and low dose immunogenic composition capable of producing a humoral and cell-mediated immunogenic response that is both systemic and tissue specific. The present invention satisfies this need.

SUMMARY OF THE INVENTION

The invention provides for immunogenic compositions and methods of use that generally include a biodegradable polyanhydride nanoparticle comprising one or more influenza virus immunogenic proteins and an adjuvant each entrapped within the interior of the nanoparticle.

In certain preferred embodiments of the invention, the immunogenic composition may comprise at least a first biodegradable polyanhydride nanoparticle formed of 1,8-bis (p-carboxyphenoxy)-3,6-dioxaoctane (CPTEG) and 1,6-bis